

PATENT

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Confirmation No.: Unassigned

Application No.: 10/635,808  
Applicant: Rapin, *et al.*  
Filed: August 5, 2003  
TC/A.AU.: Unassigned  
Examiner: Unassigned

Docket No.: NEURO 103  
Customer No.: 20786  
Title: Tripeptide Derivatives for the Treatment of  
Postlesional Diseases of the Nervous System

Commissioner for Patents  
P. O. Box 1450  
Alexandria, VA 22313-1450

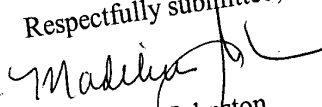
**INFORMATION DISCLOSURE STATEMENT**

Sir: The citation of information on the attached Form PTO-1449, "List of Art Cited by Applicant" is made pursuant to 37 C.F.R. §§ 1.56, 1.97, and 1.98. A copy of each reference is enclosed. The Examiner's attention is drawn to the following co-pending applications: U.S.S.N. 10/635,696; U.S.S.N. 10/635,797; and U.S.S.N. 10/635,805.

The citation of this information does not constitute an admission of priority or that any cited item is available as a reference, or a waiver of any right the applicant may have under applicable statutes, Rules of Practice in patent cases, or otherwise.

This Information Disclosure Statement is filed before receipt of a first Office action on the merits of this application, thus no fee payment as set forth under § 1.17(p) is enclosed. If any other fee is due, please charge any fees or credit any overpayment to Deposit Account No. 11-0980.

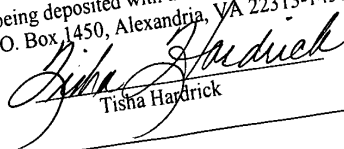
Respectfully submitted,

  
Madeline I. Johnston  
Reg. No. 36,174

King & Spalding, LLP  
191 Peachtree Street, N.E., Atlanta, GA 30303  
Office: (404)572-4600/ Fax: 404-572-5145

**CERTIFICATE OF MAILING**

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on November 25, 2003.

  
Tisha Hardrick

3342799\_6

Please type a plus sign (+) inside this box



PTO/SB/08A (08-00)  
Approved for use through 10/31/2002. OMB 0651-0031  
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

|   |   |    |   |                          |                      |
|---|---|----|---|--------------------------|----------------------|
| Substitute for form 1449A/PTO<br><br><b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br><br><i>(use as many sheets as necessary)</i> |   |    |   | <b>Complete if Known</b> |                      |
|   |   |    |   | Application Number       | 10/635,808           |
|   |   |    |   | Filing Date              | August 5, 2003       |
|   |   |    |   | First Named Inventor     | Rapin, <i>et al.</i> |
|   |   |    |   | Group Art Unit           | Unassigned           |
|   |   |    |   | Examiner Name            | Unassigned           |
|   |   |    |   | Attorney Docket Number   | NEURO 103            |
| Sheet   | 1 | of | 3 |                          |                      |

3354595\_1

| U.S. PATENT DOCUMENTS |                       |                      |                      |   |  |   |
|-----------------------|-----------------------|----------------------|----------------------|---|--|---|
| Examiner Initials *   | Cite No. <sup>1</sup> | U.S. Patent Document |                      | Name of Patentee or Applicant of Cited Document | Date of Publication of Cited Document MM-DD-YYYY | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear |
|                       |                       | Number               | Kind Code (if known) |   |  |   |
|                       | AA                    | 5,212,158            | A                    | VANDAI  | 05-18-1993                                       |   |
|                       | AB                    | 5,973,111            | A                    | BEMIS, <i>et al.</i>                            | 10-26-1999                                       |   |
|                       | AC                    | 6,156,572            | A                    | BELLAMKONDA, <i>et al.</i>                      | 12-05-2000                                       |   |
|                       | AD                    | 6,235,929            | B1                   | POWERS  | 05-22-2001                                       |   |

| FOREIGN PATENT DOCUMENTS |                       |                         |                              |                                   |   |  |   |                |
|--------------------------|-----------------------|-------------------------|------------------------------|-----------------------------------|---|--|---|----------------|
| Examiner Initials *      | Cite No. <sup>1</sup> | Foreign Patent Document |                              |                                   | Name of Patentee or Applicant of Cited Document | Date of Publication of Cited Document MM-DD-YYYY | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear | T <sup>6</sup> |
|                          |                       | Office <sup>3</sup>     | Number                       | Kind Code <sup>2</sup> (if known) |   |  |   |                |
|                          | AE                    | EP                      | 0,316,218                    | A1                                | INORGAN, S.A.                                   | 05-17-1989                                       |   |                |
|                          | AF                    | EP                      | 1,018,341                    | A                                 | CALPIS Co., Ltd.                                | 07-12-2000                                       |   |                |
|                          | AG                    | EP                      | 1,231,279                    | A1                                | CALPIS Co., Ltd.                                | 08-14-2002                                       |   |                |
|                          | AH                    | EP                      | 0,446,706                    | A2, A3                            | MERCK PATENT GESELLSCHAFT                       | 09-18-1991                                       |   |                |
|                          | AI                    | JP                      | 04-005240<br>w/ PAJ abstract | A                                 | TAISHO PHARMACEUT. Co.;                         | 01-09-1992                                       |   |                |
|                          | AJ                    | WO                      | 88/09604                     | A2                                | MEDICIS Corp.                                   | 12-15-1988                                       |   |                |
|                          | AK                    | WO                      | 92/11850                     | A2                                | CORTEX PHARMA; GA. TECH. RES. INST.             | 07-23-1992                                       |   |                |
|                          | AL                    | WO                      | 96/41638                     | A1                                | SANOFI WINTHROP                                 | 12-27-1996                                       |   |                |
|                          | AM                    | WO                      | 98/14202                     | A1                                | AUCKLAND UNISERVICES, Ltd.                      | 04-09-1998                                       |   |                |
|                          | AN                    | WO                      | 01/28578                     | A2, A3                            | WRAIR   | 04-26-2001                                       |   |                |
|                          | AO                    | WO                      | 01/34828                     | A1                                | CALPIS Co. Ltd.                                 | 05-17-2001                                       |   |                |
|                          | AP                    | WO                      | 01/68114                     | A1                                | MONSANTO Co. (US)                               | 09-20-2001                                       |   |                |
|                          | AQ                    | WO                      | 02/062373                    | A2, A3                            | TELL PHARM. AG                                  | 08-15-2002                                       |   |                |
|                          | AR                    | WO                      | 02/062828                    | A2, A3                            | TELL PHARM. AG                                  | 08-15-2002                                       |   |                |

|                    |  |                 |  |
|--------------------|--|-----------------|--|
| Examiner Signature |  | Date Considered |  |
|--------------------|--|-----------------|--|

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number. <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U. S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

Please type a plus sign (+) inside this box → ☐

PTO/SB/08A (08-00)  
Approved for use through 10/31/2002. OMB 0651-0031  
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

|  |   |    |   |                          |                |
|--|---|----|---|--------------------------|----------------|
| Substitute for form 1449A/PTO<br><br><b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b><br><br>(use as many sheets as necessary) |   |    |   | <b>Complete if Known</b> |                |
|  |   |    |   | Application Number       | 10/635,808     |
|  |   |    |   | Filing Date              | August 5, 2003 |
|  |   |    |   | First Named Inventor     | Rapin, et al.  |
|  |   |    |   | Group Art Unit           | Unassigned     |
|  |   |    |   | Examiner Name            | Unassigned     |
|  |   |    |   | Attorney Docket Number   | NEURO 103      |
| Sheet  | 2 | of | 3 |                          |                |

3354595\_1

| OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS |                       |   |                |
|---|-----------------------|---|----------------|
| Examiner Initials *                               | Cite No. <sup>1</sup> | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. | T <sup>6</sup> |
|   | BA                    | BEYER, H., and WALTER, W., <i>Handbook of Organic Chemistry</i> , by S. Hirzel Verlag, Stuttgart (English translation of the 22 <sup>nd</sup> edition of <i>Lehrbuch der Organischen Chemie</i> ) (1996), pp. 827-838.  |                |
|   | BB                    | BLUNDELL, T.L., et al., "Knowledge-based protein modelling and design", <i>Eur. J. Biochem.</i> , 172:513-520 (1988).   |                |
|   | BC                    | CHESSEBEUF, M., et al., "Rat liver epithelial cell cultures in a serum-free medium: primary cultures and derived cell lines expressing differentiated functions", <i>In Vitro</i> , 20(10):780-795 (1984).  |                |
|   | BD                    | CLARK, M.C., et al., "Validation of the general purpose Tripos 5.2 force field", <i>J. Comp. Chem.</i> , 10(8):982-1012 (1999).   |                |
|   | BE                    | DE POOTER, H., et al., "N-acylamino acids and peptides IV the synthesis of N-cinnamyl-, N-p-coumaryl- and N-cafeoyl-glycine and -glycyl-L-phenylalanine", <i>Bull. Soc. Chim. Belg.</i> , 85(9):647-656 (1976). XP008015013.                                    |                |
|   | BF                    | FADEN, A.I., et al., "Novel TRH analog improves motor and cognitive recovery after traumatic brain injury in rodents", <i>Amer. J. Physiology</i> 277(4, pt. 2):R1196-R1204 (1999), <i>Chem. Abstr.</i> 132:31033 XP002207513, XP008014976.                     |                |
|   | BG                    | FADEN, A.I., et al., "Structure-activity relationships of TRH analogs in rat spinal cord injury", <i>Brain Research</i> , 448:287-293 (1988). XP008015202.  |                |
|   | BH                    | GASTEIGER, J., et al., "Iterative partial equalization of orbital electronegativity -- a rapid access to atomic charges", <i>Tetrahedron</i> , 36:3219-3238 (1980).   |                |
|   | BI                    | HAGG, T., et al., "Delayed treatment with nerve growth factor reverses the apparent loss of cholinergic neurons after acute brain damage", <i>Exp. Neurol.</i> , 101:303-312 (1988).  |                |
|   | BJ                    | JONES, D.T., et al., "A new approach to protein fold recognition", <i>Nature</i> , 358:86-89 (July 1992).   |                |
|   | BK                    | JONES, D.T., "Protein secondary structure prediction based on position-specific scoring matrices", <i>J. Mol. Biol.</i> , 292(2):195-202 (1999).  |                |
|   | BL                    | KANSY, M., et al. "Physicochemical High Throughput Screening: Parallel Artificial Membrane Permeation Assay in the Description of Passive Absorption Processes", <i>J. Med. Chem.</i> , 41(7):1007-1010 (March 26, 1998).                                       |                |
|   | BM                    | KHUEBACHOVA, M., et al., "Mapping the C terminal epitope of the Alzheimer's disease specific antibody MN423", <i>J. Immunol. Methods (Elsevier Amsterdam, NL)</i> 262(1-2):205-215 (2002). XP004352190.   |                |

|                    |  |                 |  |
|--------------------|--|-----------------|--|
| Examiner Signature |  | Date Considered |  |
|--------------------|--|-----------------|--|

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number. <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U. S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

Please type a plus sign (+) inside this box → ☐

PTO/SB/08A (08-00)  
Approved for use through 10/31/2002. OMB 0651-0031  
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

|  |   |    |   |                          |                |
|--|---|----|---|--------------------------|----------------|
| Substitute for form 1449A/PTO<br><br><b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br><br>(use as many sheets as necessary) |   |    |   | <b>Complete if Known</b> |                |
|  |   |    |   | Application Number       | 10/635,808     |
|  |   |    |   | Filing Date              | August 5, 2003 |
|  |   |    |   | First Named Inventor     | Rapin, et al.  |
|  |   |    |   | Group Art Unit           | Unassigned     |
|  |   |    |   | Examiner Name            | Unassigned     |
|  |   |    |   | Attorney Docket Number   | NEURO 103      |
| Sheet  | 3 | of | 3 |                          |                |

3354595\_1

| OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS |                       |   |                |
|---|-----------------------|---|----------------|
| Examiner Initials *                               | Cite No. <sup>1</sup> | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. | T <sup>6</sup> |
|   | CA                    | LASKOWSKI, R.A., et al., "PROCHECK: a program to check the stereochemical quality of protein structures", <i>J. Appl. Cryst.</i> , 26:283-291 (1993).   |                |
|   | CB                    | LE PONCIN-LAFITTE, M., et al., "Sound-avoidance conditioning and a mathematical approach to the description of acquisition performance", <i>Math. Biosciences</i> , 59:249-268 (1982).  |                |
|   | CC                    | LUCO, J.M., "Prediction of the brain-blood distribution of a large set of drugs from structurally derived descriptors using partial least-squares (PLS) modeling", <i>J. Chem. Inf. Comput. Sci.</i> , 39 (2):396-404 (1999)                                    |                |
|   | CD                    | PARNETTI, L., et al., "Posatirelin for the treatment of late-onset Alzheimer's disease: a double-blind multicentre study vs citicoline and ascorbic acid", <i>Acta Neurol. Scand.</i> 92:135-140 (1995).  |                |
|   | CE                    | VARON, S., et al., "Nerve Growth Factor in CNS Repair", <i>J. Neurotrauma</i> , 11(5) (1994)  |                |
|   | CF                    | WANG, R., et al., "SCORE: A new empirical method for estimating the binding affinity of a protein-ligand complex", <i>J. Mol. Model.</i> , 4:379-394 (1998).  |                |
|   | CG                    | WEINER, S.J., et al., "A new force field for molecular mechanical simulation of nucleic acids and proteins", <i>J. Am. Chem. Soc.</i> , 106:765-784 (1984)  |                |
|   | CH                    | WIESMAN, C., et al., "Crystal structure of nerve growth factor in complex with the ligand-binding domain of the TrkA receptor", <i>Nature</i> , 401:184 (September 9, 1999).  |                |

3354595\_1

|                    |  |                 |  |
|--------------------|--|-----------------|--|
| Examiner Signature |  | Date Considered |  |
|--------------------|--|-----------------|--|

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number. <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U. S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.